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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,490	04/06/2001	Elizabeth S. Stuart	08952-008001 / UMA 00-19	5744

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,490	STUART ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-10,15,18 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-10,15,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 24, 2004 has been entered. Applicant's amendment is acknowledged. Claims 7-8, 15 and 18 have been amended. Claims 1-6, 11-14 and 16-17 have been cancelled.

2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

Rejections Withdrawn

3. The following rejections are withdrawn in view of Applicant's amendment and response.

a) rejection of claims 7-9 under 35 U.S.C. 102(b), pages 3-4, paragraph 4 of the previous Office action.

b) rejection of claims 7-10 under 35 U.S.C.103(a), pages 5-7, paragraph 5 of the previous Office action.

c) rejection of claim 18 under 35 U.S.C.103(a), pages 8-11, paragraph 6 of the previous Office action.

Rejection Maintained

4. The rejection of claim 15 under 35 U.S.C. 102 (b) is maintained for the reason of record as set forth on pages 2-3, paragraph 3 of the previous Office action.

The rejection was on the grounds Stuart et al teach purified chlamydial glycolipid exoantigen that is free of other components as determined by sodium dodecylsulfate gel electrophoreses and silver staining. The purified chlamydial glycolipid exoantigen of Stuart, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's exoantigen with the exoantigen of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the exoantigen of the prior art does not possess the same material structural and functional characteristics of the claimed exoantigen). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that claim 15 had been amended to recite a purified preparation of chlamydial glycolipid exoantigen (GLXA) and claim 15 clearly indicates that the Applicants claim a preparation of GLXA that is as a whole free of other components as determined by sodium dodecylsulfate polyacrylamide gel electrophoresis (SDS-PAGE) and silver staining. Applicant urges that Stuart et al do not teach preparations of GLXA that are free of other components. Applicant urges that the preparations of Stuart et al include GLXA and a mixture of contaminating materials. Applicant urges that the superior purity of the claimed preparation is made possible through Applicant's improved methods for isolating chlamydial glycolipids which are described throughout the specification. Applicant urges that they have amended claim 15 to further clarify the language used in the claim. Applicant urges that claim 15 as amended recites the preparation consists essentially of purified GLXA as determined by SDS gel

electrophoreses and silver staining. Applicant urges that a declaration under 37 C.F.R. 1.132 (Semprevivo Declaration) provides a side-by-side comparison of the preparations described in Stuart et al and the preparation recited in claim 15.

Applicant's arguments filed May 24, 2004 have been fully considered but they are not persuasive. The claims are drawn to a purified preparation of chlamydial glycolipid exoantigen (a product). The claim limitation "...wherein the preparation is free of other components as determined by sodium dodecylsulfate gel electrophoreses and silver staining" is a process limitation. Applicant has not distinguished the claimed product over the product of the prior art. Stuart et al teach purified chlamydial glycolipid exoantigen that is free of other components as determined by sodium dodecylsulfate gel electrophoreses and silver staining. Applicant is arguing process limitations that are not in the claims with their comments regarding the "purity" of the claimed product in comparison to the product of the prior art. There is no requirement or limitation in the claims that recite a particular level of purity that is required of the claimed product. It should be remembered that the products of the prior art reference appear to be the same or an obvious or analogous variant of the product claimed by the applicant because they appear to possess the same or similar functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 29222-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Even

if applicant's product can be shown to be of higher purity than the product of the prior art reference, applicant's needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, greater stability and/or practicality or freedom from some restrictive element or adverse side effects inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts (to which there is a basis in the specification) to applicant's product in order to overcome the aspect of the product's purity is relied upon.

In regards to Applicant's referral to the Declaration filled under 37 C.F.R. 1.132 (Declaration of Dr. Semprevivo) to point out that the preparations of the claimed invention "consists essentially of purified chlamydial glycolipid exoantigen" and preparations the prior art are not free of other components, no comparison can be made with what is presented in the Declaration. No adequate side-by-side comparison can be made from the poor quality photocopies of data (i.e. Figures 2 and 3) that were submitted with the Declaration. It should be remembered that an adequate side-by-side comparison requires that both products (i.e. the claimed product and the product from the prior art) are subjected to the same conditions and controls (i.e. run on the same gel, under the same conditions, using the same molecular weight markers for comparison and stained by the same process). Therefore, the comparison presented with the Declaration does not meet this criteria and thus an adequate comparison cannot be made. There is nothing on the record to show that the GLXA preparation of the prior art or not the same as the claimed GLXA preparation. It should be noted that

the claim recites "consisting essentially of" which is open claim language which suggest that other components that do not cause a negative effect on the claimed preparation. It is the Examiner's position that the chlamydial glycolipid exoantigen of Stuart et al are the same as the chlamydial glycolipid exoantigen preparations of the prior art. Therefore, Stuart et al anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 7-9 and 18-19 are rejected under 35 U.S.C. 103(a) as unpatentable over Whittum-Hudson et al *(Nature Medicine, October 1996, 2(10), 1116-21)* in view of Dick, Jr. et al *(Conjugate Vaccine, Contrib. Microbiol Immunolo. Basel., Karger 1989, Vol. 10, pp. 48-114).*

Claims 7-9 and 18-19 are drawn to a composition comprising a carrier group covalently coupled to an isolated chlamydial glycolipid oligosaccharide.

Whittum-Hudson et al teach that the chlamydial exoglycolipid antigen (GLXA) is expressed at all differentiation stages of the *Chlamydia* organisms and is secreted from infected cells (page 1116, 2nd column). Whittum-Hudson et al teach that GLXA is an unique chlamydial antigen. Whittum-Hudson et al teach that the antigenic

determinants of GLXA resides on it polysaccharide component thus making it a T-independent antigen, as such GLXA will not be expected to generate protective IgG antibody responses or T-helper cell responses (page 1116, 2nd column). Whittum-Hudson et al teach GLXA is specific for the 89MS30 antibody therefore, GLXA is capable or binding the 89MS30 antibody (page 1117, 2nd col). Whittum-Hudson et al teach that anti-idiotypic antibodies have been suggested as alternatives to purified antigens as vaccine candidates particularly when antigen preparation is technically difficult as for tumor-specific antigens or bacterial carbohydrate antigens (page 1117, 1st column). Whittum-Hudson et al teach that anti-ID to GLXA represents both functional and molecular mimicry of GLXA, it induces anti-GLXA responses and according to competitive inhibition studies mimics the combining sites of monoclonal antibody mAb_1 and antibody Ab_3 for GLXA (page 1117, 1st column). However, Whittum-Hudson et al also teach that the use of anti-Id for infectious agents has been limited in part because of the difficulty in delivery of antibodies to the mucosal immune system, particularly as fed vaccines (page 1117, 1st column).

Whittum-Hudson et al teach do not teach a carrier group covalently coupled to the GLXA.

Dick, Jr. et al teach that conjugation of bacterial carbohydrate antigens to a carrier protein. Dick, Jr. et al teach that some subjects (e.g. children under 18 months and elderly people) fail to produce antibodies when stimulated with capsular polysaccharide immunogens (CPS) at level too low to be protective (page 49). Dick, Jr. et al teach that high-risk populations retain the ability to produce protective antibodies

against immunogenic proteins such as diphtheria toxoid or tetanus toxoid by a process that can be adapted to carbohydrate antigens (page 49). Dick, Jr. et al teach that proteins and polysaccharides are classified into two separate classes of antigens thymus dependent (TD) and thymus independent (TI) antigens, respectively (page 49). Dick et al teach that polysaccharides classified as TI antigens have multiple repeat epitopes on their polymeric chains which collectively bind and cross-link immunoglobulin receptors on the surface of B cells and the net effect is the induction of cellular differentiation processes that yield antibody-producing plasma cells (page 49). Dick, Jr. et al teach that it is well established that covalent bonding of carbohydrate antigens demonstrate a thymus dependent (TD) response to carbohydrate components (page 49 and 58). Dick, Jr. et al teach that CPS can be linked to carrier proteins directly or by bifunctional linkers (spacer arms) (pages 71-72) which overcome conjugation limitations imposed by steric effects (page 71). Dick, Jr. et al teach that linkers can promote improved antigenicity for the bound components as compared to results obtained when testing the same antigens conjugated by a direct method (page 72). Dick, Jr. et al teach that spacers (i.e. linkers) permit corresponding increases in translational and rotational characteristics of the antigens, increasing access of the binding sites to soluble antigens (page 72). Dick, Jr. et al teach that linkers can be covalently bound to carbohydrate components (page 70).

It would be *prima facie* obvious at the time the invention was made to use covalently couple the oligosaccharide/polysaccharide of chlamydial GLXA as taught by Whittum-Hudson et al to a carrier protein (e.g. diphtheria toxoid or tetanus toxoid) as

taught by Dick, Jr. et al because Whittum-Hudson et al teach that GLXA is abundant in *Chlamydia* species as well as being antigenic and Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins thereby, demonstrating a thymus dependent (TD) response to carbohydrate components and enhancing the immune response to carbohydrate component. It would be expected barring evidence to the contrary, a composition comprising GLXA covalently coupled to a carrier protein would be effective in stimulating a response from the immune system since the polysaccharide component has been demonstrated to be antigenic. One of skill in the art would have been motivated to produce the immunogen as combined because Whittum-Hudson et al that the use of anti-Id for infectious agents has been limited in part because of the difficulty in delivery of antibodies to the mucosal immune system, particularly as fed vaccines.

6. Claim 10 is rejected under 35 U.S.C. 103(a) as unpatentable over Whittum-Hudson et al *(Nature Medicine, October 1996, 2(10), 1116-21)* and Dick, Jr. et al *(Conjugate Vaccine, Contrib. Microbiol Immunolo. Basel., Karger 1989, Vol. 10, pp. 48-114)* as applied claims 7-9 and 18-19 *supra* and further in view of Semprevivo *(Carbohydrate Research, 1988, 177, p. 222-227).*

Claim 10 is drawn to the composition of claim 9, wherein the linker is 2-(4-aminophenyl)ethylamine.

The teachings of Whittum-Hudson and Dick, Jr. et al have been described above.

The combination of Whittum-Hudson et al and Dick, Jr. et al as set forth *supra* does not teach that the linker is 2-(4-aminophenyl)ethylamine.

Semprevivo teaches 2-(4-aminophenyl)ethylamine linkers. Semprevivo teaches that oligosaccharides behave as simple haptens and must be linked either to proteins or a solid support in order to raise and isolate a specific antibody (see the Abstract). Semprevivo teaches that all oligosaccharides regardless of size become associated with the carrier protein (page 225). Semprevivo teaches that coupling oligosaccharides with a 2-(4-aminophenyl)ethylamine linker conserves that chemical integrity of the oligosaccharide.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the 2-(4-aminophenyl)ethylamine linkers as taught by Semprevivo to covalently bond the carrier group (diphtheria toxoid or tetanus toxoid) to the oligosaccharide of Whittum-Hudson et al and Dick, Jr. et al as combined above because Semprevivo has demonstrated that 2-(4-aminophenyl)ethylamine linkers can be used to form oligosaccharide-protein conjugates (see the Abstract). One would be motivated use of 2-(4-aminophenyl)ethylamine linkers to produce the claimed chlamydial glycolipid-oligosaccharide conjugated of because 2-(4-aminophenyl)ethylamine teach the 2-(4-aminophenyl)ethylamine can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Additionally, Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins to enhance the immune response to the response to carbohydrate component.

7. Claim 10 is rejected under 35 U.S.C. 103(a) as unpatentable over Whittum-Hudson et al *(Nature Medicine, October 1996, 2(10), 1116-21)* and Dick, Jr. et al *(Conjugate Vaccine, Contrib. Microbiol Immunolo. Basel., Karger 1989, Vol. 10, pp. 48-114)* as applied to claims 7-9 and 18-19 *supra* and further in view of Smith et al (*Journal of Biological Chemistry, 255(1), 1980, p. 55-59*).

Claim 10 is drawn to the composition of claim 9, wherein the linker is 2-(4-aminophenyl)ethylamine.

The teachings of Whittum-Hudson et al and Dick, Jr. et al have been described above.

The combination of Whittum-Hudson et al and Dick, Jr. et al as set forth *supra* does not teach that the linker is 2-(4-aminophenyl)ethylamine.

Smith et al teach the β-(p-aminophenyl)ethylamide (i.e. 2-(4-aminophenyl)ethylamine) can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Smith et al teach the coupling of oligosaccharides to bovine serum albumin and keyhole limpet hemocyanin (see the Abstract). Smith et al teach that rabbits immunized with the synthetic glycoproteins produced antibodies directed against the oligosaccharides (see the Abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the β-(p-aminophenyl)ethylamide (i.e. 2-(4-aminophenyl)ethylamine) linkers as taught by Smith et al to covalently bond the carrier

group (diphtheria toxoid or tetanus toxoid) to the oligosaccharide of Whittum-Hudson et al and Dick, Jr. et al as combined above because Smith et al have demonstrated that β-(p-aminophenyl)ethylamide linkers can be used to form oligosaccharide-protein conjugates (see the Abstract). One would be motivated use of β-(p-aminophenyl)ethylamine linkers to produce the claimed chlamydial glycolipid-oligosaccharide conjugated of because Smith et al teach the β-(p-aminophenyl)ethylamide (i.e. 2-(4-aminophenyl)ethylamine) can be used to couple proteins via their phenylisothiocyanate intermediates under conditions that preserve labile sugar linkages (see the Abstract). Additionally, Dick, Jr. et al teach that carbohydrate components can be covalently linked to carrier proteins to enhance the immune response to the response to carbohydrate component.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 18 recite the term "capable of". It is unclear as to what the applicant is referring? Claims limitations should be definite. "Capable of" is a potential suggesting that a claim limitation may or may not take place. Clarification is required.

Status of Claims

9. No claims allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vanessa L. Ford
Biotechnology Patent Examiner
July 27, 2004

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